TESTIMONY TO THE HOUSE SUBCOMMITTEE ON HEALTH

RE: THE THREAT OF, AND PLANNING FOR, PANDEMIC FLU

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Summary

- The World Health Organization (WHO) and influenza experts worldwide warn that an influenza virus (flu) pandemic is inevitable and imminent and will likely be caused by widespread distribution of an avian influenza virus, e.g. avian flu.

- Vaccines are the mainstay of prophylaxis against influenza, but there is currently no vaccine capable of protecting humans from infection with avian flu.Currently approved anti-viral drugs may be useful to treat pandemic flu but their effectiveness is limited by development of resistance.

- Novel and new anti-viral approaches are required to enhance the effectiveness of existing anti-viral drugs, prevent viral resistance to existing drugs, and to provide a strategy to combat avian flu and other important respiratory viral diseases.

- The discovery of RNA interference, or RNAi has revolutionized our ability to offer new, potent and specific viral disease intervention. RNAi is a natural biological process that occurs in all of our cells. The process is mediated by the activity of short strands of RNA that specifically silence the targeted gene of interest.

- We have harnessed the power of RNAi to silence respiratory virus infection and disease by targeting viral genes. We have shown that RNAi is very potent, specific, and reactive for all strains of virus targeted.

- RNAi is a new breakthrough solution to address pandemic flu that is on the horizon. Support for this new and proven technology will provide an unprecedented means to control pandemic flu and other important respiratory virus infections that carry a high disease burden on mankind.

Pandemic Influenza (flu):

- A pandemic is an epidemic that spreads rapidly around the world with high rates of illness and death. While people are exposed to different strains of the flu virus many times in their lives, about three or four times every century a radically different strain of flu causes a pandemic.
- Such warnings by the World Health Organization, Centers for Disease Control, National Institutes of Health and Institute of Medice have been fueled by the persistence of a highly virulent strain of avian influenza virus in Asia that experts fear could trigger another influenza pandemic.
- Influenza pandemics are not new. In the 20th century, mankind has faced three influenza pandemics. The first was the devastating 1918 "Spanish Flu" pandemic, as well as two less severe influenza pandemics in 1957 and 1968.

Key facts of pandemic flu:

- Pandemic flu occurs every few decades and spreads rapidly to affect most countries and regions around the world. Unlike the 'ordinary' flu that usually occurs every winter, pandemic flu can occur at any time of year
- Pandemic flu is much more serious than 'ordinary' flu - as much as a quarter of the population may be affected - maybe more.
- A serious pandemic is also likely to cause many deaths, disrupt the daily life of many people and cause intense pressure on health, poultry and other industries.

What is pandemic flu caused by?

- The emergence of a new flu virus which is markedly different from recently circulating strains and to which few people have any immunity.

Strategies to protect against pandemic flu:

- Vaccines are the mainstay of prophylaxis against influenza, but there are technical and safety issues that must be overcome, and problems in producing sufficient vaccine to meet global requirements. There is no vaccine ready to protect against pandemic flu.
- Currently approved anti-viral drugs can be used to treat pandemic flu but their effectiveness is limited by development of drug resistance.

The nature of the next pandemic flu: *Avian Influenza*:

- WHO and influenza experts worldwide are concerned that the recent appearance and widespread distribution of an avian influenza virus, influenza A/H5N1 (H5N1) "has the potential to ignite the next pandemic", World Health Organization, December 2004.

What is *Avian Influenza*?

- Avian influenza is a contagious disease of birds and poultry caused by influenza A viruses. All bird species are susceptible to infection, but domestic poultry flocks are especially vulnerable. Infection can cause epidemics associated with severe illness, high death rates, and economic devestation.

Where does *Avian Influenza* occur?

- Avian flu occurs worldwide. The current outbreak of highly pathogenic avian flu (H5N1) began in Asia and has to date affected poultry in nine countries in Asia. In three of these countries, H5N1 strain has also infected people.

How does *Avian Influenza* spread?

- Avian flu is spread in poultry flocks either via respiratory secretions or contact with contaminated droppings. People are usually infected through close contact with infected birds or their feces. Person-to-person spread, so far appears to difficult.

Protecting the human population from *Avian Influenza*:

- There is currently no vaccine capable of protecting humans from infection, and effectiveness of exisiting anti-virals is not well understood.

Why I am here today:

- I am here today to tell you about the emerging pandemic threat from avian influenza virus and how scientists at the University of Georgia are developing novel therapeutics with Alnylam Pharmaceuticals, Cambridge, MA to treat and prevent avian influenza and other important respiratory viral infections.
- My concerns echo those of the Centers for Disease Control, National Institutes of Health, the World Health Organization, and Institute of Medicine which all warn of the need for pandemic flu preparedness, particularly for avian influenza.

What is the potential impact of Avian Influenza?

- The emergence of new influenza A virus subtypes have caused all three known flu pandemics, all of which spread around the world within 1 year of being detected.
- *1918-19, "Spanish flu"*, [H1N1]: caused the highest number of known influenza deaths: more than 500,000 people died in the United States, and up to 50 million people may have died worldwide. Nearly half of those who died were young,

healthy adults. Influenza A (H1N1) viruses still circulate today after being introduced again into the human population in the 1970s.

- *1957-58, "Asian flu,"* [H2N2], caused about 70,000 deaths in the United States. First identified in China in late February 1957, the Asian flu spread to the United States by June 1957.
- 1968-69, *" Hong Kong flu,"* [H3N2), caused about 34,000 deaths in the United States. This virus was first detected in Hong Kong in early 1968 and spread to the United States later that year. Influenza A (H3N2) viruses still circulate today.

Historical patterns and influenza:

- Influenza pandemics can be expected to occur, on average, three to four times each century when new virus subtypes emerge and are readily transmitted from person-to-person.
- Pandemic flu spreads rapidly. During the pandemics of 1957 and 1968, the viruses took only 3-4 months to spread from southeast Asia – where they were first identified – to Europe and North America.
- Today, conditions are far more favorable to the spread flu. With high population density, and ease of air travel around the world, an outbreak could spread to virtually every city in the world in a matter of a few days.

Influenza virus disease intervention strategies:

- Multiple approaches will be required to protect the human population from newly emerging influenza virus strains such as H5N1 and others.
- Vaccines are the mainstay of prophylaxis against influenza, but there are technical and safety issues that must be overcome.

- Anti-viral agents have been shown to be effective toward treating influenza subtypes; however, avian flu (H5N1) is resistant to two common influenza drugs, rimantadine and amantadine, but newly developed drugs such as Tamiflu and Relenza appear to be somewhat effective.
- *The evidence for viral resistance to anti-viral agents indicates that more than one drug will be necessary to combat influenza.*

Novel new anti-viral approaches – **RNA Interference (RNAi)**:

- New anti-viral drugs are required to enhance the effectiveness of current drugs and prevent drug resistance.
- In my laboratory at the University of Georgia, we are working with new breakthrough technology called ***RNA interference, or RNAi.*** RNAi is a natural biological process that occurs in all of our cells to control development. RNAi is mediated by the activity of short strands of RNA that specifically silence the targeted gene of interest.
- We have harnessed the power of RNAi to silence respiratory virus infection and disease by targeting viral genes. We have shown that RNAi is very potent, specific, and reactive for all strains of virus targeted. We have shown that RNAi prophylaxis and therapeutic treatment can be used to effectively silence respiratory syncytial virus (RSV) which is the leading cause of serious lower respiratory tract in infants and young children worldwide.
- RNAi has the potential to create powerful therapeutics that meet the demand for new drugs with higher potency, lower toxicity, and have a high degree of specificity, i.e. only attack their target and do so very efficiently.

RNAi and the pending threat of pandemic flu:

- It is absolutely necessary that our disease intervention strategies move beyond the standard vaccine and into a new class of *proven* preventative and therapeutic treatments. With RNAi, the creation of a safer, more accurate and efficient anti-viral treatment for pandemic influenza is closer in reach.
- Specific anti-viral RNAi therapeutics can be developed rapidly, i.e. within several months, produced at high levels, and stock piled or stored as needed.
- RNAi is a new breakthrough solution to address pandemic flu that is on the horizon. Support for this new and proven technology will provide an unprecedented means to control pandemic flu and other important respiratory virus infections that carry a high disease burden on mankind.

Clearly, without support for this robust research program that can prevent respiratory virus disease burden, and silence virus replication and spread, we are doomed to relive the pandemics of the past. In developing the RNAi disease intervention strategies, we are developing tools to respond to any novel virus that may emerge.